Amendments to the Specification:

Please replace the paragraph beginning at page 1, line 4, with the following amended paragraph:

This application is a continuation-in-part of U.S. Serial No.: 08/861,338, filed May 21, 1997, now U.S. patent 6,174,993, the entire teachings of which are incorporated herein by reference.

Please replace the paragraph beginning at page 1, line 15, with the following amended paragraph:

As such, phosphorylation of serine or threonine by serine/threonine kinases is an important mechanism for regulating intracellular events in response to environmental changes. A wide variety of cellular events are regulated by serine/threonine kinases. A few examples include the ability of cells to enter and/or complete mitosis, cellular proliferation, cellular differentiation, the control of fat metabolism, immune responses, inflammatory responses and the control of glycogen ~~metebolism~~ metabolism.

Please replace the paragraph beginning at page 2, line 6, with the following amended paragraph:

It has now been found that short peptides which are derivatives of the HJ loop of a serine/~~theonine~~threonine kinase can significantly affect the activities of cells expressing the serine/threonine kinase ("HJ loop" is defined

hereinbelow). For example, the peptide ~~drivatives~~ derivatives of the HJ loop of Raf and Polo inhibit the proliferation of bovine aortic cells and the transformed mouse cell lines MS1 and/or SVR cells *in vitro* at concentrations as low as 10 μM (Example 2). Based on the aforementioned discoveries, novel peptides are disclosed herein which are peptide derivatives of the HJ loop of serine/threonine kinases. Also disclosed are methods of identifying a peptide derivative of an HJ loop of a serine/threonine kinase which modulates the activity of said serine/threonine kinase. Methods of modulating the activity of a serine/threonine kinase in a subject are also disclosed.

Please replace the paragraph beginning at page 3, line 10, with the following amended paragraph:

The peptides of the present invention can be used in the treatment of a wide variety of diseases caused by overactivity and underactivity of a STK. Examples include, but are not limited to, cancer, diabetes, obesity, diseases of the central nervous system, inflammatory disorders, autoimmune ~~dieseases~~ diseases and cardiovascular diseases. The peptides of the present invention also have *in vitro* utilities, for example, in the generation of antibodies which specifically bind the serine/threonine kinase from which the peptide was derived. These antibodies can be used to identify cells

expressing the serine/threonine kinase and to study the intracellular distribution of the serine/threonine kinase. In addition, the peptides of the present invention can be used to identity and quantitate ligands which bind the HJ loop of the serine/threonine kinase from which the peptide was derived.

Please replace the paragraph bridging pages 17 and 18 with the following amended paragraph:

In another aspect, the activity of certain STK (e.g., Atk/PKB, Dudek *et al.*, *Science* 275:661 (1997)) can be evaluated by growing the cells under serum deprivation conditions. Cells are typically grown in culture in the presence of a serum such as bovine serum, horse serum or fetal calf serum. Many cells, for example, nerve cells such as PC-12 cells, generally do not survive when there is insufficient serum. The use of insufficient serum to culture cells is referred to as "serum deprivation conditions" and includes, for example, from 0% to about 4% serum. STK activity is determined by the extent to which a peptide or peptide derivative can protect cells, e.g., neuronal cells, from the consequences of serum deprivation. Specific conditions are provided in Dudek et al., and in Example 4 of co-pending and concurrently filed application entitled "SHORT PEPTIDES WHICH SELECTIVELY MODULATE INTRACELLULAR SIGNALLING" U.S. Patent Application No. 08/861,153,filed on May 21, 1997, now patent

no. 6,723,694, the teachings of which are incorporated herein by reference.

Please replace the paragraph bridging pages 18 and 19 with the following amended paragraph:

Generally, the activity of the STK in the test mixture is assessed by making a quantitative measure of the cellular activity which the STK controls. The cellular activity can be, for example, cell proliferation. Examples of cells in which proliferation is controlled by an STK include endothelial cells such as bovine aortic cells, mouse MSI cells or mouse SVR cells (see Arbiser *et al.*, *Proc. Natl. Acad. Sci. USA 94*:861 (1997)), vascular smooth muscle cells, and malignant cells of various tissues such as breast cancer, lung cancer, colon cancer, prostrate cancer, melanoma~~)~~. STK activity is assessed by measuring cellular proliferation, for example, by comparing the number of cells present after a given period of time with the number of cells originally present. STKs involved in cell proliferation are members of the polo family, Taf or Atk/PKB. If cells are being used in which the STK controls the cell ~~differentitiation~~ differentiation (e.g., preadipocytes such as 3T3-L1 expressing STKs Akt/PKB, GSK3 and protein kinase A--see Kohn *et al.*, *J. Biol. Chem. 271*:31372 (1996)), activity is assessed by measuring the degree of differentiation. Activity can be

assessed by changes in the metabolic activity of cells such as primary adipocytes, hepatocytes and fibroblasts by measuring changes in glucose uptake, lipogenesis, or glycogen metabolism (see, for example, Weise *et al.*, *J. Biol. Chem.* *270*:3442 (1995)). Activity can also be assessed by the extent to which the gene expression, cell morphology or cellular phenotype is altered (e.g., the degree to which cell shape is altered or the degree to which the cells assume a spindle-like structure). One example of a change in cellular morphology is reported in the ~~co-pending and concurrently filed application~~ patent 6,723,674, entitled "SHORT PEPTIDES WHICH SELECTIVELY MODULATE INTRACELLULAR SIGNALLING", ~~U.S. Patent Application No. 08/861,153, filed May 21, 1997,~~ which discloses that certain peptide derivatives of the HJ loop of protein tyrosine kinases can cause vascular smooth muscle cells to become elongated and assume a spindle-like shape.

Please replace the paragraph beginning at page 22, line 14, with the following amended paragraph:

With respect to obesity, an improved clinical outcome refers to increased weight reduction per ~~calory~~ calorie intake. It also refers to a decrease in the complications which are a consequence of obesity, for example heart disease such as arteriosclerosis and high blood pressure.

Please replace the paragraph beginning at page 25, line 12, with the following amended paragraph:

Protein tyrosine kinases are another class of protein kinases. These proteins occur as membrane-bound receptors, which participate in transmembrane signaling, or as intracellular proteins which take part in signal transduction within the cell, including signal transduction to the nucleus. Binding of a ligand results in signal transduction, initiated by the phosphorylation of tyrosine residues of intracellular proteins by the kinase. As with STKs, tyrosine kinases control cellular functions by means of this phosphorylation mechanism. Tyrosine ~~kinaes~~ kinases have a high degree of homology with STKs, including an HJ loop. Consequently, the activity of tyrosine kinases and the cellular functions which they control, can be modulated with peptides which are peptide derivatives of their HJ loops, as discussed above for STKs. Peptides and peptides derivatives of the HJ loop of protein tyrosine kinases and methods of use thereof are disclosed in ~~the co-pending and concurrently filed application entitled "SHORT PEPTIDES WHICH SELECTIVELY MODULATE INTRACELLULAR SIGNALLING"~~ U.S. Patent 6,723,694 ~~Application No. 08/861,153, filed May 21, 1997~~, the teachings of which are incorporated into this application.